PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below
International application No. PCT/EP2005/000542	International filing date *(day/month/year)* 20.01.2005
Priority date *(day/month/year)* 21.01.2004	
International Patent Classification (IPC) or both national classification and IPC C07D417/04, C07D417/14, A61K31/501, A61K31/506, A61P11/00	
Applicant NOVARTIS AG	

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/000542

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-14
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-14
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1- Reference is made to the following documents cited in the search report:

d1: WO 99/64418 A (NOVARTIS AG; NOVARTIS-ERFINDUNGEN VERWALTUNGSGESELLSCHAFT MBH; HENG, R) 16 December 1999 (1999-12-16)

d2: WO 03/039451 A (FUJISAWA PHARMACEUTICAL CO., LTD; TSUTSUMI, HIDEO; TABUCHI, SEIICHIRO;) 15 May 2003 (2003-05-15)

d3: WO 02/42298 A (NOVARTIS AG; NOVARTIS-ERFINDUNGEN VERWALTUNGSGESELLSCHAFT MBH; PRESS,) 30 May 2002 (2002-05-30)

2- Novelty

Present compounds are novel at least on account of the group Y.
The requirements of Art. 33.2 are therefore met.

3- Inventive step

3.1- The applicant has set himself the task of providing novel compounds which exhibit inhibition of A2b receptor activation.
Documents d1 and d3 relate to thiazole derivatives having the same use of present compounds. D2 discloses thiazole derivatives showing greater affinity for the A1 and A2a receptors (cf. page 36). Considering the chemical structures of the compounds disclosed in these documents and their activity, it is considered that d1 represents the closest state of the art.
For the purpose of assessing the inventive step during the international phase, it is accepted that present compounds of formula (I) have the claimed activity, i.e. they inhibit the activation of the A2a receptor.

3.2- Compounds of d1 differ from the compounds of the invention in that the thiazole is substituted in position 5 by a pyridine ring while in the corresponding position, present compounds contain a pyrimidine or pyridazine ring. Despite this similarity, it appears that there are no suggestions in the prior art documents for replacing the pyridine by a

pyrimidine or pyridazine moiety according to the present group Y.
Hence, present compounds are regarded as inventive.